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LOW ELECTRICAL SKIN RESISTANCE IN THE REGION OF PAIN IN PAINFUL ACUTE SINUSITIS*

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Received for publication October 6, 1949

Objective signs of pain are of obvious importance, particularly when communication with the patient is imposible or untrustworthy. Such signs may be found by careful examination of accessible areas of referred pain in visceral disease. Here it may be possible to map out areas of hyperaesthesia, muscle spasm, abnormal sweating, vasomotor changes, and areas of increased pilomotor activity (1). Any technic which makes this examination more delicate should be useful. Such signs as abnormal sweating, vasomotor changes, and increased pilomotor activity suggest the existence of sympathetic hyperactivity in the region of referred pain. Study of electrical skin resistance offers an extremely sensitive method for demonstrating areas of sympathetic hyperactivity (2). This method will pick up changes in sympathetic activity which the physical senses of the examiner cannot. It might be useful, therefore, in the examination of areas of referred pain.

Painful sinusitis affords an ideal testing ground for determining the value of the skin resistance method in studying areas of referred pain. The disease can be diagnosed accurately. Definite pain is referred to the surface of the body. Various therapeutic procedures give relief from pain without interferring with the skin of the pain reference area. It is possible, therefore, to obtain accurate measurements of skin resistance before and after relief of pain.

It was decided, therefore, to study electrical skin resistance in the region of pain in painful acute sinusitis. This is a preliminary report containing observations on nine patients.

*Carried out under a contract between the Office of the Surgeon General of the U.S. Army and The Johns Hopkins University.

†Captain, MC, U. S. Army, stationed at Heidelberg, Germany.

MATERIALS AND METHODS

Skin resistance was measured with a 22.5 volt dermometer (3) in the manner described by Richter and Woodruff (4).

The dermometer circuit consisted of a 22.5 volt battery, a rheostat to regulate the voltage applied to the patient and a microammeter which registered change in resistance of the skin. This was connected to the patient by means of two electrodes. One of these electrodes was painted with Cambridge Electrode Jelly and secured to the patient's ear lobe. This ear lobe had been previously punctured with a needle in the area of attachment of the electrode. Therefore, this electrode was in contact with the highly conductive fluids of the body. The second electrode was movable and could be brought into contact with the skin of any portion of the body. Because of the attachment of the first electrode to the conducting fluids of the body, the resistance of the skin beneath this movable electrode was the resistance measured by the dermometer (2).

In these experiments the dermometer was not used to measure actual resistance, but rather to indicate changes in resistance as the movable electrode was moved from place to place on the skin. The current from the batteries was so adjusted that when the movable electrode was placed over areas of high resistance, the ammeter pointer moved no more than a few divisions on the dial. Consequently, when the electrode was placed over areas of lower resistance, the pointer moved further across the dial. By using the rheostat to regulate the current properly it was possible to determine the points of highest skin resistance, the points of lowest skin resistnce, and the points of skin resistance which were at various intermediate levels between the two extremes.

The skin resistance pattern of the face was mapped out by the following procedure. The movable electrode was placed in contact with the skin of the upper part of the forehead, which has a comparatively high resistance. The rheostat was set so that the current from the batteries scarcely deflected the ammeter pointer. Then the movable electrode was moved towards the center of the face, touching the skin at points one-half inch apart. A close watch was kept on the ammeter pointer for a sharp deflection which would show that an area of low skin resistance had been reached. By moving the electrode back and

forth between areas of high and low resistance at successively smaller intervals, it was possible to determine quite accurately the point at which the resistance dropped. This point was marked with a skin marking pencil. This process was repeated on other parts of the face until by joining all of the points together the boundary of the entire area of low resistance could be defined. Then the area of low resistance was explored using a similar rheostat setting to make sure that the area

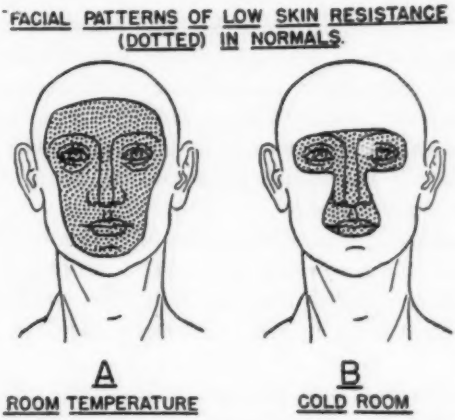

FIG. 1. Facial pattern (stippled) of low electrical skin resistance in normal individuals.

A. Shows the large type of pattern seen when the subject is in a warm environment or when excited.

B. Shows the constricted type of pattern seen when the subject is in a cold environment (55°F). The pattern may become even smaller and involve only the mouth and lips. These normal patterns are invariably symmetrical.

contained no islands of high resistance. Finally, the rheostat was adjusted so that the current from the batteries scarcely deflected the ammeter pointer when the electrode was at the outskirts of the area of low resistance. The low resistance area was then further explored in order to detect areas of still lower resistance. This procedure was continued until the high, intermediate, and low resistance areas of the entire face had all been mapped.

The skin of the normal face shows a sharply demarcated symmetrical

area of low electrical resistance which usually includes both eyelids, the nose, the mouth, and varying portions of the forehead, of the cheeks, and of the skin of the lower lip. This area varies in size according to the external temperature (Fig. 1). In warm environments the area of low skin resistance may dilate to include the skin of the entire face. In cold temperatures the area becomes progressively smaller until it includes only the mouth and lips. This area is called the normal facial pattern of low skin resistance (4).

A large normal facial pattern of low skin resistance often overlaps the area of referred pain. It could interfere with the detection of abnormal low skin resistance in the painful area. Therefore, the patients were cooled in a cold room (55°F) or with an electric fan in order to reduce the normal facial pattern to the smallest possible size. By use of this procedure it was possible to remove the normal facial pattern from the area of referred pain.

Using the methods described above, the facial skin resistance pattern was determined in nine consecutive cases of acute sinusitis which were seen at the Johns Hopkins Hospital, Baltimore, Maryland, and the General Dispensary, U. S. Army, Pentagon Building, Washington, D. C.

Since morphine and most other analgesics have a marked effect on the electrical skin resistance, the patients were examined before they received any form of medication.

RESULTS

An abnormal area of low skin resistance was found in the region of pain in each of the nine consecutive cases of painful acute sinusitis. These abnormal low resistance areas disappeared after the pain went away in the seven cases that were followed.

Fig. 2 shows these results in more detail. The drawings labeled 'A' show the typical distribution of pain in each case (solid black shading). This is entirely typical of the type of sinusitis involved. The drawings labeled 'B' show the low facial skin resistance patterns while pain was present. These (stippled) asymmetrical patterns have two components: first, the symmetrical normal facial pattern of low skin resistance; second, a sharply demarcated area of low skin resistance that in some manner is associated with the pain. It may be con-

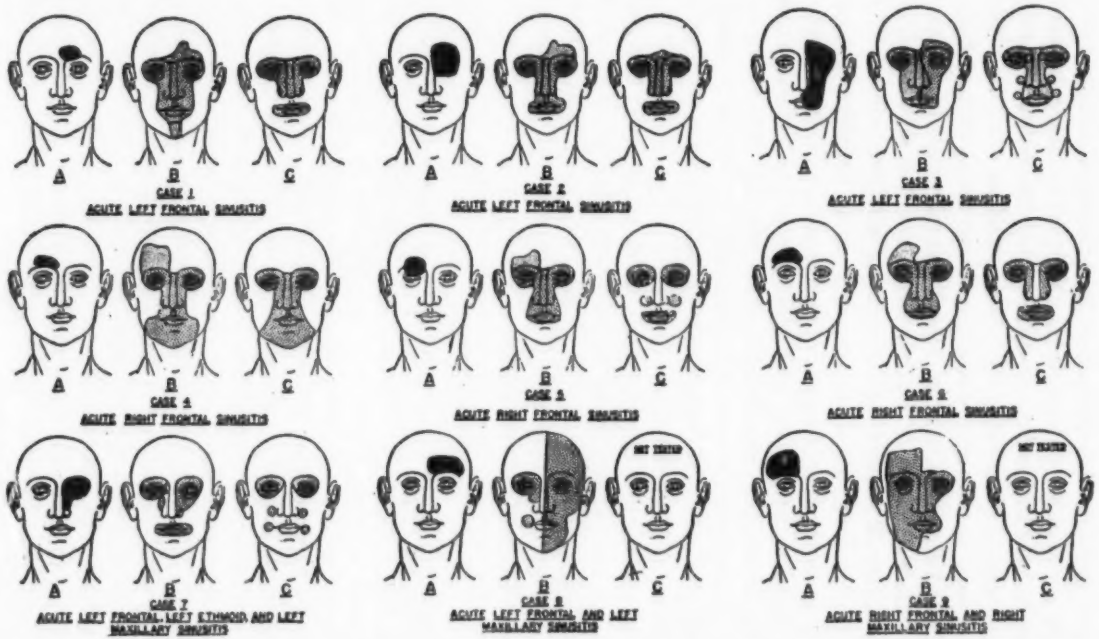

FIG. 2. Data on the 9 cases of acute sinusitis. In each instance drawing 'A' shows the distribution of pain, drawing 'B' shows the electrical skin resistance pattern while pain was present, and drawing 'C' shows the skin resistance pattern after pain had disappeared.

tiguous to or partially superimposed on the symmetrical facial pattern. The resistance in this painful area may be equal to (case 8,9), lower than (case 3, 7), or higher than (case 1, 2, 4, 5, 6) the resistance found in the symmetrical facial pattern of low skin resistance. The drawings labeled 'C' show the low skin resistance patterns after pain had disappeared (stippled). These patterns are all normal symmetrical facial patterns of low resistance. The abnormal areas of low skin resistance seen in drawing 'B' have disappeared along with the pain. It is of interest that although all of the mappings on an individual patient were done under the same external environmental conditions, the symmetrical facial pattern of low skin resistance is small when pain is absent. Sinus pain, therefore, seems to cause two skin resistance phenomena: (a) an abnormal area of low skin resistance which is located in the region of pain and (b) a symmetrical enlargement of the normal facial pattern of low resistance.

Physical examination detected evidence of sympathetic hyperactivity in only one patient. In case 8, visible hyperhydrosis was noted in the region of pain and abnormal skin resistance. This patient was not followed and consequently it is not known what happened to the hyperhydrosis after relief of pain.

DISCUSSION

The findings reported above have not been observed in studies of the facial skin resistance patterns in a very large number of patients without acute sinusitis. Therefore, it is reasonable to presume from the data advanced that abnormal areas of low skin resistance can be found in the region of pain in acute painful sinusitis. It is probable that this area of low skin resistance is due to sympathetic hyperactivity in the region of referred pain. In favor of this possibility is the large body of evidence showing that the resistance of intact skin varies with sympathetic activity, particularly of the sweat glands, being highest when sympathetic activity is low or is eliminated by sympathectomy, and being lowest when sympathetic activity is high (2). The visible hyperhydrosis present in the area of pain in case 8 may be further evidence of local sympathetic hyperactivity. However, the lack of information on what happened to this patient after pain was relieved limits the value of this evidence.

These areas of abnormal low skin resistance in the region of sinus pain may prove to be of considerable value in the diagnosis of sinusitis. However, further studies will be necessary first to indicate: (a) whether such areas can be found in all painful cases of sinusitis; (b) whether they are present in cases of painless sinusitis; (c) whether they may be present in cases with facial pain due to causes other than sinusitis. Additional investigation is called for to determine whether these findings in referred sinus pain will be present in referred pain from any viscus.

CONCLUSIONS

An abnormal area of low skin resistance was found in the region of pain in each of nine consecutive cases of painful acute sinusitis. In the seven cases that were followed these low resistance areas disappeared after the pain was removed.

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AGGLUTINATION OF RED CELLS ALTERED BY THE ACTION OF NEWCASTLE DISEASE VIRUS*

I. The Effect of Chicken Sera from Infected Birds on Sensitized Cells

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Received for publication Oct. 11, 1949

The immediate response of a host in adjusting to an invading virus is not yet undestood, so that changes in the sera in the acute phase of an infection are of particular interest. Burnet and Anderson in 1946 (1) described a phenomenon in which human red cells, previously "sensitized" by the virus of Newcastle Disease of chickens, were then agglutinated by the sera of patients having infectious mononucleosis. They suggested this might indicate a serological relationship between the two diseases. Although agglutination of Newcastle-sensitized cells by sera from cases of infectious mononucleosis has not been consistently demonstrated in this country, the peculiar ability of certain sera from other diseases to agglutinate these sensitized cells has been demonstrated (2). It was also shown by the Australian workers that an agglutinin of sensitized chicken cells was present in the sera of chickens infected with Newcastle Disease. We have studied particularly the phenomenon in the chicken and have defined the conditions under which it occurs. It is a property of serum taken early in the course of active disease and not in the convalescent stage.

"Sensitization" of either human or chicken red cells is achieved by exposing a concentrated cell suspension to the action of a suspension of Newcastle virus in an incubator for 2 hours.† During this time virus has presumably been adsorbed on and subsequently released from the red cells. The cells are then washed 3 times in saline. A suspension of these cells may be shown to be altered in that they will no longer be

*Supported in part by a Grant in Aid from the National Institutes of Health, U.S.P.H.S.

†The original description of Burnet and Anderson calls for 1/2 hour, but in our experience 2 hours produced more stable cells.

agglutinated by a second exposure to the virus. These sensitized cells can, however, be agglutinated by certain sera which do not agglutinate normal cells.

In this paper we will consider the agglutination of sensitized chicken cells by sera from acutely infected chickens and the factors which influence this agglutination. In a later paper we will consider the agglutination of human "O" cells by human sera and similar factors influencing this agglutination.

The results fall into three general groups. First is an evaluation of the method of performing the test; secondly the study of the time during the illness of the chicken when the test is positive, and thirdly an attempt to study some of the characteristics of the substance present in chicken sera causing the agglutination.

METHOD

In the performance of the actual test, normal cells obtained at the same time from the same bird, and which have received the same treatment except for exposure to virus, are run as controls. Except where specifically indicated, tests were run at 4°C. One of the variables in the test is the preparation of stable sensitized cells, i.e. cells which will not spontaneously agglutinate. Preliminary experiments indicate that the time of shaking, the degree of aeration, and perhaps exposure to glass, all influence this stability.

Since the virus titer of the supernatant fluid after incubation equals the titer of the original virus suspension (3), and since no definite virus particles have been seen by electron microscopy to adhere to the red cells (4), it may be assumed that few intact virus particles remain on the red cells.

Preparation of Sensitized Cells—We have two strains of Newcastle virus under continuous study in the laboratory. One of these ("B") is relatively avirulent, but is an excellent agglutinator of chicken red cells. The other, (CG179), though highly virulent for 8-week old chickens, is a poor and inconstant agglutinator of red cells. (5) Recently in connection with the effect of the virus on human cells, we have obtained from Dr. A. S. Evans the original Australian strain of virus used by Burnet and Anderson.

A comparison of the sensitivity of cells treated by these three strains is presented in Table I. All three strains of virus did sensitize cells as shown by their reactivity with various sera. In general the strain of virus producing the highest

titer of agglutination of red cells was the bset sensitizing virus, and the poorest agglutinator produced the least sensitive cells.

The degree of adsorption of the virus on the red cell might influence the outcome. A comparison of the adsorption of the three strains of virus on chicken

TABLE I

Sensitizing Effect of Three Different Strains of Newcastle Disease Virus

	CELLS SENSITIZED BY			
	S	B	Cg	Australian
Chicken Sera Acute Phase of Newcastle Disease + Sensitized Chicken Cells	1	80	10	
	2	2560		640
	3	160		40
Human Sera + Sensitized Human "O" Cells (Atypical Pneumonia)	1	160	80	
	2	10	0	
	3	10	2	
Chicken Cell Agglutinin Titer of Virus Preparations Used		1280–2560	0–20	320

All figures refer to highest dilution causing 2+ agglutination.

TABLE II

Effect of Exposure of Varying Dilutions of Freshly Harvested Virus to a One Per Cent Suspension of Washed Chicken Cells for Varying Periods of Time

STRAIN OF VIRUS	DILUTION OF ALLANTOIC FLUID EXPOSED	CONTROL	20 MINUTES	40 MINUTES
B* (agglutinator)	1/10	9.2	8.8	
	1/100	8.7		8.5
Cg (poor agglutinator)	1/10	8.5	8.3	
	1/10	8.7	7.7	8.5
Australian	1/10	9.3	9.3	8.7
	1/100	9.3	7.3	

* Data for this strain previously published (5).

All figures refer to the log of the 50% infectivity end point.

cells fails to show any correlation with the sensitivity of treated cells. This may however be due to the crudeness of the infectivity titrations, which are probably not accurate below 0.6 log.

It is indicated later that some positive human sera lost titer on remaining at 4°C. This loss is less in chicken sera. However, we have

frozen all sera in order to preserve it. Freezing and thawing had little apparent effect on the chicken sera (Table III).

During the course of our experiments with human sera it was found that tests which were run at 4°C yielded much higher titers than those

TABLE III

Effect of Freezing for 6 Days and Thawing on Acute Phase Sera Titer

CELLS FOR CHICKEN #	SERUM TESTED AFTER	1/10	1/20	1/40	1/80	1/160	1/320	1/640	1/1280	1/2560	1/5120
	24 hours in										
	Deep freeze −16°C	+++	+++	+++	+++	+++	+++	+	0	0	0
	Quick freeze	+++	+++	+++	+++	+++	+++	+	0	0	0
	CO_2 (−70°C)	+++	+++	+++	+++	+++	+++	+++	+	0	0
	Icebox (4°C)	+++	+++	+++	+++	+++	+++	0	0	0	0
#37 Sensitized	6 days in										
	Deep freeze −16°C	+++	+++	+++	+++	+++	+++	+++	0	0	0
	Quick Freeze	+++	+++	+++	+++	+++	+++	+	0	0	0
	CO_2	+++	+++	+++	+++	+++	+++	++	+	0	0
	Icebox	+++	+++	+++	+++	+++	++	+	0	0	0
#37 Normal	6 days in										
	Deep Freeze	0	0	0	0	0	0	0	0	0	0
	Quick Freeze	+	0	0	0	0	0	0	0	0	0
	CO_2	+	0	0	0	0	0	0	0	0	0
	Icebox	0	0	0	0	0	0	0	0	0	0
#73 Sensitized	6 days in										
	Deep freeze	+++	+++	+++	+++	+++	+++	++	0	0	0
	Quick freeze	+++	+++	+++	+++	+++	+++	+++	++	0	0
	CO_2	+++	+++	+++	+++	+++	+++	++	+	0	0
	Icebox	+++	+++	+++	+++	+++	+++	++	+	0	0
	24 hours in Icebox	0	+++	+++	+++	+++	+++	+++	++	0	0

TABLE IV

*Effect of Temperature on Agglutination of Sensitized Chicken Cells**

TEMPERATURE	DILUTION OF ACUTE PHASE SERA								
	1/20	1/40	1/80	1/160	1/320	1/640	1/1280	1/2560	1/5120
4°C	+++	+++	+++	+++	++	+	0	0	0
20–23°C	++	++	+++	+++	+	0	0	0	0
35°C	+++	+++	++	+	0	0	0	0	0

* All of same dilutions were tested against normal cells and were negative throughout.

run at approximately 25°C. A study of the effect of temperature on the test with chicken sera vs. sensitized chicken red cells is presented in Table IV. As may be seen the effect is minimal.

In an attempt to find some of the variable factors in the tests we tablulated the results of the same sera agains cells from different chick-

TABLE V

Effect of Source of Chicken Red Cells on the Titer of Various Sera

Figures in Table refer to the Final Dilution of Sera which produced a 2+ Agglutination of Sensitized Cells.

INDIVIDUAL SERA FROM CHICKENS INFECTED FOR	CELLS FROM CHICKEN #				
	190	103	138	69	73
6 days	640	80			
6 days		320			
		160*			
7 days	160				
	320*		160		
7 days	320			160	
7 days	40			20	1280
7 days			5120	80	
				320*	6120
7 days				320	320
8 days	160				
	80*				

* Repeated after freezing and thawing one more time.

TABLE VI

Sensitivity of Different Chicken Cell Preparations Treated with the Same Virus at the Same Time

CELLS FROM CHICKEN #		SERUM OF 7TH DAY INFECTION									
		10	20	40	80	160	320	640	1280	2560	5120
Sensitized	73	+++	+++	+++	+++	++	0	0	0	0	0
	43	+++	+++	+++	+++	+++	0	0	0	0	0
	38	+++	+++	+++	+++	+++	++	+	0	0	0
	37	+++	+++	+++	+++	+++	+++	+++	+++	++	0
	26	+++	+++	+++	+++	+++	+++	+++	++	0	0
Unsensitized	73	0	0	0	0	0	0	0	0	0	0
	43	0	0	0	0	0	0	0	0	0	0
	38	0	0	0	0	0	0	0	0	0	0
	37	0	0	0	0	0	0	0	0	0	0
	26	+++	+++	++	0	0	0	0	0	0	0
	92	+++	+++	+++	+++	+++	++	+	0	0	0

ens (Table V). This shows a striking difference depending on the source of the preparation. This is better shown in Table VI where the tests were run simultaneously. Included in this test is the effect of the

same sera on unsensitized cells from the same chickens. The cells from one of these are partially agglutinated, as are the cells of an older chicken (#92) which had been repeatedly bled in the past. This sensitivity of untreated red cells from a chicken which has been repeatedly bled may become so great that a saline suspension of these washed cells will form a spontaneous pattern in the bottom of the tube. The de-

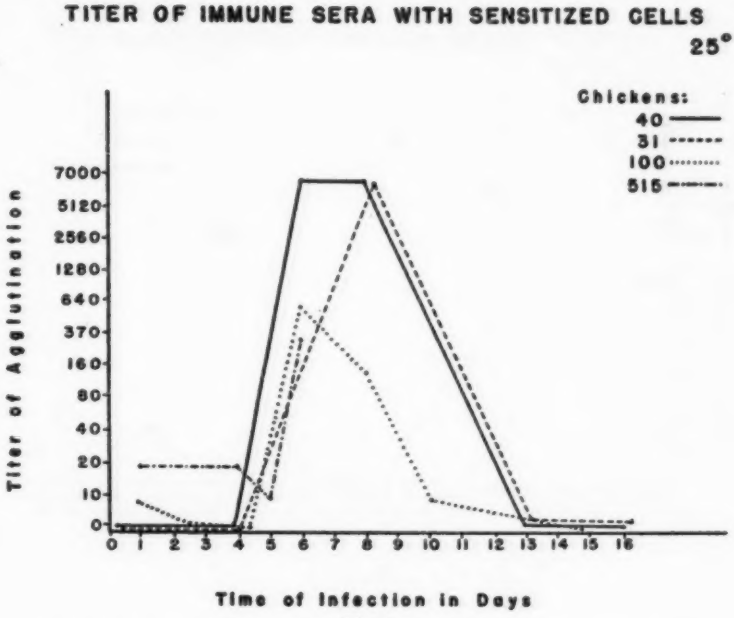

Fig. 1

velopment of auto-agglutination of rabbit cells in the sera of rabbits repeatedly bled may be a somewhat similar phenomenon (7). The individual variable susceptibility of chicken cells has been noted in several other virus-red cell systems (8, 9, 10).

It was early noted (1) and confirmed (2) that when various animals including chickens were injected with the viruses of Newcastle or influenza, there developed in their serum a substance capable of agglutinating sensitized cells. It has not been determined whether

or not this virus needs to be living. However, no study of the time of its appearance and disappearance in the blood of such chickens, and no attempt to differentiate it from antibody has appeared.

As may be seen in Figs. 1 and 2, the titer of this agglutinin of sensitized red cells rises sharply on about the 5th–6th day and is present particularly during the acute phase of the animal's illness. On the other hand, antibody hemagglutinin-inhibition rises perhaps a little

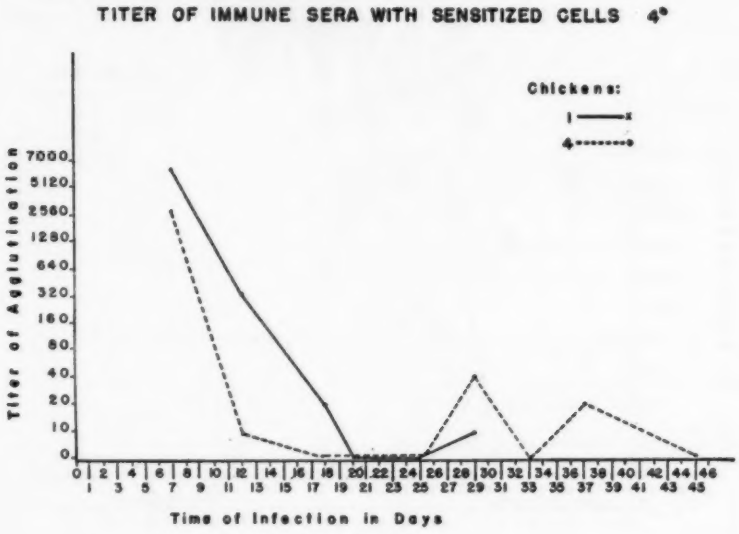

Fig. 2

later and then, as is to be expected, is maintained for at least six weeks (Fig. 3).

Since the agglutinin for sensitized cells is present only during the acute phase of the infection, as distinct from antibody, we attempted to determine something of its characteristics.

We found that the agglutinin obtained from acute phase sera will not dialyze through a collodion bag, that it does not precipitate when dialyzed against saline or 2 to 3 changes of water, but that it finally does come down in the precipitate with continued changes of water over a 2 day period. This is with an estimated dilution of the original

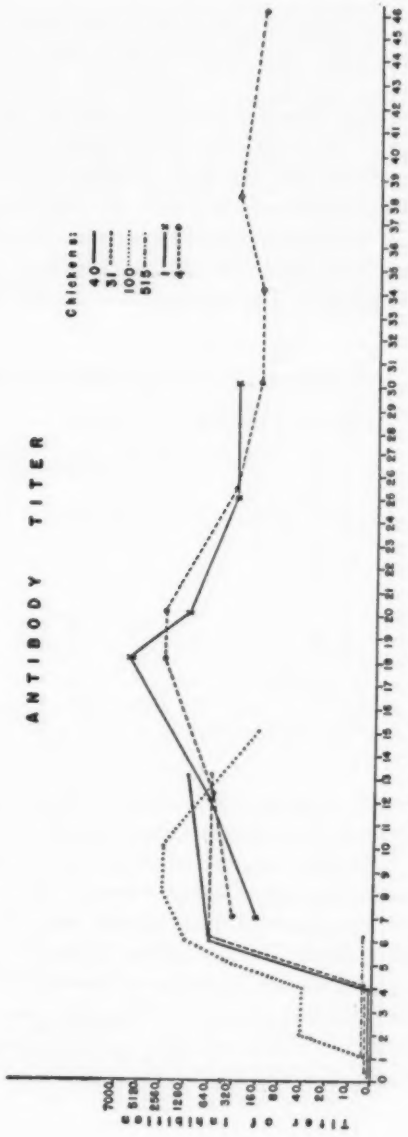
ANTIBODY TITER
Chickens:
40
31
100
515
1
Time of Infection in Days
TITER OF INHIBITION
7000
5120
2560
1280
640
320
160
80
40
20
10
0

Fig. 3

saline of 1/20. There was some loss of activity on dialysis which was not restored by combining precipitate and supernatant and the dialysate.

It has been shown that normal chicken red cells are capable of agglutinating sensitized chicken red cells. We were interested in determining wherein this factor resided and, therefore, hemolysed both normal chicken and normal human red cells. It is interesting (Table VII) that human cell hemolysate produced agglutination in a 1/320 dilution whereas the ghosts produced agglutination in a 1/8 dilution of the original 1% suspension. The hemolysate from chicken red cells

TABLE VII

Agglutination of Sensitized Cells by Hemolysate and Red Cell Ghosts of Human and Chicken Origin

HEMOLYSATE 1%	1/10	1/20	1/40	1/80	1/160	1/320	1/640	1/1280	1/5120	1/10,240
Human hemoglobin	+++	+++	+++	+++	+++	+++	0	0	0	0
Fowl #1	0	0	0	0	0	0	0	0	0	0
Fowl #2	0	0	0	0	0	0	0	0	0	0
	1%	1/2	1/4	1/8	1/16	1/32	1/64	1/128	1/512	1/1024
Human ghosts	+++	+++	+++	+++	0	0	0	0	0	0
Fowl #1	+++	+	0	0	0	0	0	0	0	0
Fowl #2	+++	+++	+++	+++	0	0	0	++	++	++

failed to agglutinate any sensitized red cells in a 1/10 dilution or more, whereas one preparation of the ghosts agglutinated in a 1/8 dilution of the original 1% suspension and the other only in the original 1%. It would seem then that the agglutinating substance is liberated from human red cells by hemolysis in much greater amounts than from fowl red cells. This is similar to the pecten antagonist of influenza virus-agglutination extracted by Wooley from hemolysates of chicken and human red cells (11). The presence of this agglutinin of sensitized red cells in the ghosts of chicken red cells is also reminiscent of the influenza virus hemagglutin inhibitor which has been extracted from

this same source by Hirst (12). The relationship of the agglutinin from normal red cells and that from the acute phase sera has not been studied.

The presence in the blood of a proteolytic enzyme whose activity varies during the course of various diseases, including infections (13), led us to test the effect of commercial trypsin, papain, and purified trypsin* on these sensitized cells.

TABLE VIII

Agglutination of Sensitized Red Cells by Proteases

	1/10	1/20	1/40	1/80	1/160	1/320	1/640	1/1280	1/2560	1/5120
Sensitized cells										
Unpurified tyrpsin	0	+	+++	+++	+++	+++	+++	+	++	++
	1%	1/2	1/4	1/8	1/16	1/32	1/64	1/128	1/256	1/512
1% Purified trypsin	+++	+++	+++	+++	+++	+++	+++	0	0	0
Chloroform treated chicken sera	0	0	0	0	0	0	0	0	0	0
Normal sera #174	0	0	0	0	0	0	0	0	0	0
Normal Cells										
Unpurified trypsin	0	0	0	0	0	0	0	0	0	0
	1%	1/2	1/4	1/8	1/16	1/32	1/64	1/128	1/256	1/512
1% Purified trypsin	0	0	0	0	0	0	0	0	0	0
Chloroform treated chicken sera	0	0	0	0	0	0	0	0	0	0
Normal sera #174	0	0	0	0	0	0	0	0	0	0

The results of these tests are shown in Table VIII wherein it is demonstrated that sensitized cells are much more sensitive to the agglutinating action of trypsin both purified and relatively crude. Similar results were obtained with papain. This does not indicate that the agglutinin of sensitized cells is such an enzyme. Pertinent to this is the failure of chloroform treatment (14) of normal chicken serum† to liberate such an agglutinin. Such treatment of human serum will liberate the proteolytic enzyme by destruction of its inhibitor. Furthermore, the effect of trypsin can be inhibited by soy bean inhibitor which has no effect on the titer of the agglutinin in the sera.

*Courtesy Dr. M. Kunitz

†Courtesy of Dr. O. D. Ratnoff

The agglutinin of sensitized red cells in chicken serum is relatively heat stable for no loss of activity was demonstrated after heating at 56°C for one half hour, but activity began to decrease after two hours exposure to this temperature (Table IX).

One of the first enzyme inhibitors tested was cyanide, at concentrations varying from .0005 M. to .005 M. An effect was consistently present until the concentration of the phosphate buffer in the saline was increased whereupon it disappeared, even when .005 M CN was used. Furthermore, the original cyanide effect was not reversed by .05% methylene blue. The effect of variation in the pH of the medium

TABLE IX

The Effect of Heating at 56°C Upon Agglutinin of Sensitized Cells

EXP.		DILUTION OF SERA									
		1/10	1/20	1/40	1/80	1/160	1/320	1/640	1/1280	1/5120	1/10,240
1	½ hrs. Heated normal sera	0	0	0	0	0	0	0	0	0	0
	Unheated norm. sera	+	+	+	+	0	0	0	0	0	0
	Heated immune sera	+++	+++	+++	+++	++	+	0	0	0	0
	Unheated immune sera	+++	+++	+++	+++	+++	+	0	0	0	0
2	2 hrs. Heated normal sera	+++	+	0	0	0	0	0	0	0	0
	Unheated norm. sera	+++	+++	0	0	0	0	0	0	0	0
	Heated immune sera	+++	+++	+++	++	+	0	0	0	0	0
	Unheated immune sera	+++	+++	+++	+++	+++	++	+	0	0	0

was then studied in the range pH 5.0 to 8.9. A slightly greater effect of alkaline concentrations on the sensitized reaction is apparent.

Choline esterase is mentioned by some as a participant in the reaction of influenza virus with red cells (15). Di-iso fluoro phosphate, a specific inhibitor of this enzyme, had no effect on the agglutinin titer.

Carbon monoxide (commercial gas bubbled through the saline before the addition of the sensitized red cells) and methylene blue in a concentration of .05% had no effect on the reaction. .005 M hydroquinone did not change the reaction, whereas .005 sodium azide lowered it slightly. This, like the cyanide reaction, may have been due to a higher pH.

TABLE X

Effect of Variation in pH on the Hemagglutination Reaction

INHIBITION OF VIRUS	DILUTION OF SERA										
	pH	1/10	1/20	1/40	1/80	1/160	1/320	1/640	1/1280	1/2560	1/5120	C
Hemagglutination by Immune Sera	5.04	++	+	0	0	0	0	0	0	0	0	0
	5.80	+	+	0	0	++	++	+++	+++	+++	+++	+++
	5.90	0	0	0	+	++	+++	+++	+++	+++	+++	+++
	6.30	0	0	0	0	++	+++	+++	+++	+++	+++	+++
	6.99	++	+	0	0	0	++	+++	+++	+++	+++	+++
	7.51	0	0	0	0	0	+++	+++	+++	+++	+++	++
	7.72	0	0	0	0	++	+++	+++	+++	+++	+++	++
	8.31	0	0	0	0	0	0	0	0	0	0	0
	8.95	+++	0	0	+	++	+++	+++	+++	+++	+++	++
Agglutination of Sensitized Cells by sera	5.04	+++	+++	+++	+++	+	+	0	0	0	0	0
	5.80	+++	+++	+++	+++	+++	+	0	0	0	0	0
	5.90	+++	+++	+++	+++	+++	+++	+++	++	+	0	0
	6.30	+++	+++	+++	+++	+++	+++	+++	++	0	0	0
	6.99	+++	+++	+++	+++	+++	+++	+	+	0	0	0
	7.51	+++	+++	+++	+++	+++	+++	++	0	0	0	0
	7.72	+++	+++	+++	+++	+++	+++	0	0	0	0	0
	8.31	+++	+++	+++	+++	+++	0	0	0	0	0	0
	8.95	+++	+++	+++	+++	++	0	0	0	0	0	0
Agglutination of Normal Cells by sera	5.04	+++	++	0	0	0	0	0	0	0	0	0
	5.80	0	0	0	0	0	0	0	0	0	0	0
	5.90	+	0	0	0	0	0	0	0	0	0	0
	6.30	0	0	0	0	0	0	0	0	0	0	0
	6.99	0	++	0	0	0	0	0	0	0	0	0
	7.51	++	0	0	0	0	0	0	0	0	0	0
	7.72	++	0	0	0	0	0	0	0	0	0	0
	8.31	+	0	0	0	0	0	0	0	0	0	0
	8.95	++	+	0	0	0	0	0	0	0	0	0
Agglutination of Red cells by Virus Alone	5.04	++	0	0	0	0	0	0	0	0	0	
	5.80	0	0	0	0	0	0	0	0	0	0	
	5.90	0	0	0	++	+++	+++	++	0	0	0	
	6.30	+++	+++	+++	+++	+++	+++	+++	++	0	0	
	6.99	+++	+++	+++	+++	+++	+++	++	0	0	0	
	7.51	+++	+++	+++	+++	+++	+++	++	0	0	0	
	7.72	+++	+++	+++	+++	+++	++	0	0	0	0	
	8.31	+++	+++	+++	+++	+++	+++	++	0	0	0	
	8.95	+++	+++	+++	+++	+++	+++	++	0	0	0	

DISCUSSION

The phenomenon of agglutination of red cells by certain viruses is in itself a complex mechanism. The problem has been extended by the discovery that certain cells, following exposure to virus, become sensitive to agglutination by certain sera and extracts of red cells. For the purpose of thinking about the action of Newcastle Disease

virus on red cells we have considered the problem in several stages. The phenomenon of agglutination here is basically one of making the red cells sticky. Unlike cells exposed to the virus of influenza, red cells exposed to the virus of Newcastle Disease do not settle more rapidly than normal cells. Even with preparations of allantoic fluid containing Newcastle Virus titering to 5,000 by hemagglutination this is true. Furthermore, as indicated at the beginning of the paper, actual adsorption of virus on the cell even with very active preparations may be minimal. Therefore, adsorption of virus of red cells, and agglutination of those red cells as they settle to the bottom of the tube, may well be independent factors. It may also be that the elution of virus from the red cells, and the sensitizing action on the red cell, are separate factors.

For these reasons we felt that the demonstration that sera taken from chickens infected with Newcastle disease allowed a more extensive analysis of the phenomenon than would be possible by studying a series of patients. Furthermore, the incomplete characterization of the serum component and its action at least allows certain things to be excluded.

It should, however, be emphasized that we have as yet no knowledge of whether the reaction between infectious mononucleosis sera and human red cells sensitized to Newcastle virus is fundamentally the same as the one here studied or not. The presence of this factor in acute sera with its disappearance in convalescent sera tends to rule out ordinary antibody (though various types of incomplete antibodies are not ruled out). Its heat stability and preservation in the icebox eliminates complement. The occasionally marked difference in sensitivity of red cells from different chickens raises the question of the role of antigens uncovered by the process of sensitization and differing from one chicken to another. Finally, the repetition of the phenomenon with certain parts of the hemolyzed human and chicken red cell turns one's thoughts towards inhibitor-like substances.

SUMMARY

Chicken red cells "sensitized" by exposure to Newcastle virus may be agglutinated by sera and red cell hemolysates which do not agglutinate normal red cells. Four approaches have been used in trying

to understand this phenomenon: The effects of (1) different temperatures, (2) different strains of virus, (3) cells from different chickens, and (4) the occurrence and stability of the agglutinating sera.

Sera taken from chickens five to seven days after they are inoculated with avirulent Newcastle virus will agglutinate "sensitized" cells, but fail to agglutinate normal cells. This characteristic of the sera does not obtain during the subsequent few days of the chicken's convalescence, antibodies (anti-virus hemagglutinins) having meanwhile appeared and persisted.

The factor in the serum responsible for the agglutination of sensitized cells is resistant to a temperature of 56°C for one hour, it does not dialyze through a collodion bag, it is preserved for 13 months in a frozen state, and is partially precipitated by dialysis against distilled water.

Sensitized cells were agglutinated by a hemolysate of human red cells and by the washed ghosts of normal chicken cells.

Attempts to characterize the factor by some of the usual enzyme inhibitors failed. Proteases, such as purified and crude trypsin and crude commercial papain agglutinated sensitized chicken cells and not normal cells in the concentrations used. This agglutination was inhibited by soybean inhibitor. However, chloroform treatment of normal sera which in mammalian sera releases the fibrinolytic enzyme, failed to produce an agglutinin of sensitized cells, and soybean inhibitor of trypsin did not inhibit agglutination by the positive chicken sera.

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SPINAL SUBDURAL ABSCESS DUE TO A CONGENITAL DERMAL SINUS AND ACCOMPANYING CHANGES IN THE AUTONOMIC NERVOUS SYSTEM*

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The following case of a congenital dermal sinus with an accompanying spinal subdural abscess has all the characteristic sensory and motor changes that Walker and Bucy included under their clinicopathological entity (1). The case ran essentially the same course as did those described by Walker and Bucy, by List (2), and by Freedman and Alpers (3). In addition this case presents wide-spread and long lasting autonomic effects, objective records of which were obtained by means of the electrical skin resistance method.

Previous papers give a full description of the electrical skin resistance mapping method and of the underlying principles (4). It will suffice to state here that the electrical resistance of the skin varies inversely with the activity of the sympathetic nervous system: a high skin resistance indicating little or no sympathetic activity; a low resistance indicating marked sympathetic activity. The dermometer used for the test consisted of either a $4\frac{1}{2}$ or $22\frac{1}{2}$ volt battery, a 1000 ohm potential divider, and a 50 microammeter. One electrode was attached to an ear lobe by means of a small silver plated nickel clasp; the other, an exploring electrode, consisting of a silver plated disc or solid metal roller attached to a wooden handle, was held in the hand of the examiner and so could be moved from place to place on the skin.

This dermometer was used only to define the boundaries of areas with various levels of increased or decreased sympathetic activity, not to obtain an actual measurement of skin resistance in ohms.

*Carried out under a contract between the Office of the Surgeon General of the U. S. Army and The Johns Hopkins University.

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D. L. E.: First admission: June 14 to August 17, 1944

This one year old girl was admitted with paralysis of both legs. The illness had started when she was 2 weeks old and a small draining sinus was noticed in the midline of the lower back. The fluid that drained from the sinus was at first clear, but after 6 months changed to pus. Three months later the sinus was excised. Following operation the operative site drained profusely for a short time but healed completely by the end of 6 weeks. The child remained well for several weeks, then became weak in the legs. This condition progressed until 2 weeks before admission when both legs became totally paralyzed.

On admission the temperature was 103.6° and the child was restless and uncooperative. The abdomen was markedly distended with a huge bladder. Catheterization yielded 460 cc of urine. In the lower lumbar region in the midline an indurated area was present and the tiny opening in its center was not draining. Horner's syndrome was present on the right side. There was a loss of sensation on the right side from the nipple down, and on the left from the inguinal region down. The knee and ankle jerks were absent on both sides.

Laminectomy performed by Dr. F. Otenasek revealed the presence of a huge intradural abscess. This was opened and drained. The child improved immediately; profuse drainage present for a few days quickly receded. Recurrent bladder infection and constipation constituted the main post-operative difficulties. An indwelling catheter was required until August 8. After this she had to be catheterized 3 times daily. Daily doses of mineral oil relieved the constipation. The infection was treated with penicillin and sulfadiazine.

By the time of discharge the child was able to walk when aided and the urinary infection had cleared up.

Interval Note: October, 1944. Two months after discharge the child was seen again. She had improved steadily. Walking with slight support was possible. The right side of the body from the head to the umbilicus did not perspire. The child still had no bladder control. The abdominal reflexes on the right were diminished. The tendon reflexes in the right leg were still absent.

Second Admission: November 6–27, 1947. The child was not seen

again until November 1947, when she was admitted to the Johns Hopkins Hospital for the second time at the request of her local physician.

Since last seen, the child had made remarkable recovery. She had grown normally, and had had no illnesses of any kind, except for recurrent bladder infections. Since the age of 2 years she had been walking alone. The child was alert, active, and bright. She was still incontinent of urine. Her mother catheterized her three times daily. Constipation remained a problem. The lumbar sinus continued to exude a few drops of pus daily.

Physical Examination: Temperature, pulse and respiration were normal. A long midline scar was present over the lumbar spine. In the region of L_4 there was a small mound of granulation tissue with a sinus in the center from which a drop of pus could be expressed. The right leg appeared to be about 2 cm. shorter than the left. On standing, there was a scoliosis with an upward tilt of the pelvis on the right.

Neurological examination showed no discrepancy in the cranial nerves. The Horner's syndrome was no longer present. Muscle strength, tone and movement were unimpaired in the arms. In the legs, however, there was marked hypotonus on the right. The muscles were not as well developed as on the left, the right thigh being 2 cm. less, and the calf being $1\frac{1}{2}$ cm. less in circumference than the corresponding parts on the left. Strength in all muscle groups was less than on the left and the joints were relaxed. The right ankle was unstable and dorsiflexion poor. The toes could not be moved voluntarily. On the left, strength and tone were much better but there was definite weakness of dorsi and plantar flexion of the foot.

The child was cooperative and accurate on sensory examination. Touch was intact, as were deep pressure and position senses. Vibration was lost at the ankles but appreciated at the knees. Pain sensibility was diminished on the right everywhere below the umbilicus; it appeared to be lost on the posterior aspect of leg and over the buttock. On the left pain appreciation was diminished over S_2 and absent over the buttock. There were no cerebellar difficulties. The tendon reflexes in the arms were intact. The abdominal reflexes on the right could not be obtained. The right knee kick was diminished and the right

ankle jerk was absent. The corresponding reflexes on the left were normal. No pathological reflexes were obtained.

There was a limp on walking and the right leg was used as a prop. The right ankle tended to evert. The leg was strong, however, and would bear her weight. The back was limber and could be bent in all directions without discomfort.

Leucocyte count showed 18,000 cells per cu. mm. X-rays of the lumbar regions showed that the spinous processes of the 3rd and 4th lumbar spines were missing. There was no evidence of bone destruction or of osteomyelitis.

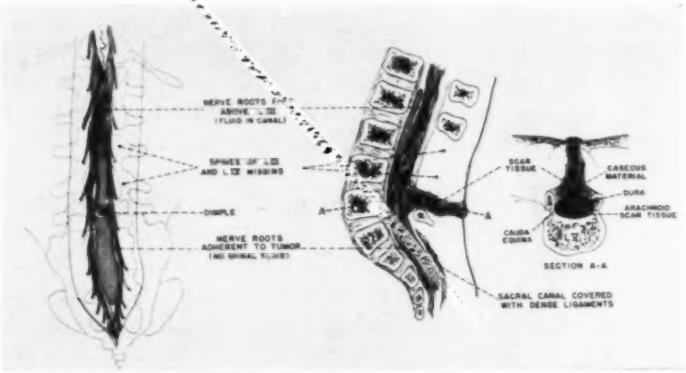

FIG. 1. Drawing made at the operating table showing the sinus within the dural space.

The sinus was injected with thorotrast and the opaque material filled the sacral portion of the spinal canal. On November 12, 1947, the old laminectomy incision was opened. The sinus tract was excised as a core, and followed down into the spinal canal. It ran through the dura, where it was connected with a long sausage-shaped mass, which extended from L_1 to the coccyx (See drawing in Fig. 1). The roots were adherent to the outside of the mass by dense arachnoid tissue, but were not incorporated in it. In order to expose the tumor it was necessary to remove the lamina at $L_{1,2,5}$ ($L_{3,4}$ having been previously removed). The sacral canal was covered with ligamentous tissue only. It was possible to remove the tumor completely without

injury to the roots except for a few of the lower sacral filaments. Pathological study of the mass showed that it was a cystic tumor lined with stratified squamous epithelium.

The post-operative course was uneventful. The wound healed per primum without evidence of infection. It was necessary to catheterize the child for several days. She was able to walk with support on the 8th post-operative day and by the date of discharge on November 27, 1947 she could once more walk alone. The neurological status was unchanged. Cystemetric study of the bladder showed increased capacity but good tone and normal tracing. It was noted that there was no pain or desire to void when the bladder was distended.

Interval Notes: January 26, 1948. The patient walks well but with a limp, using the right leg as a prop. She still is unable to move the toes of the right foot and has only slight control of movements of the right ankle. Feels pain as far down as S_1 on the right, no anesthesia on the left. Has better control of bladder and bowel.

June 7, 1948. Patient has continued to improve. The knee and ankle jerks are still absent on the right side. She has some voluntary control of movements on right foot. The right leg is 1 cm. shorter than the left.

April 29, 1949. In the standing position the patient's right foot is is slightly everted. She walks well but with a limp. Her right knee and ankle jerks are still absent. She is able to extend the small toes of the right foot, but has no power in the extensor hallucis longus or the anterior tibial muscle groups. The right peroneal muscles are quite strong. The hamstring muscles of the right leg are approximately 50% of normal strength. Plantar flexion of the right ankle is approximately 30% of normal strength. The patient has developed considerable control of her urinary bladder and rectal sphincter.

Electrical Skin Restance Examination:

This patient was examined 8 times over a period of 5 years beginning with an examination on the day of admission. Fig. 2 shows the skin resistance patterns that were found on three different occasions.

June 14, 1944. This examination made on the day of admission revealed a sharply defined unilateral area of increased skin resistance (decreased sympathetic activity) that included the entire right half

of the body. A line at T_9 sharply divided an upper area with a very high resistance (solid black) from a lower area with only an intermediately high resistance (cross hatching). Above this line the resistance was as high as is found after a complete sympathectomy.

June 7, 1948. This examination made 4 years after the initial admission revealed a sharply defined unilateral area of increased resistance that still included the entire right side of the body (except for small facial area). The magnitude of the increase in resistance was much smaller than that present in 1944.

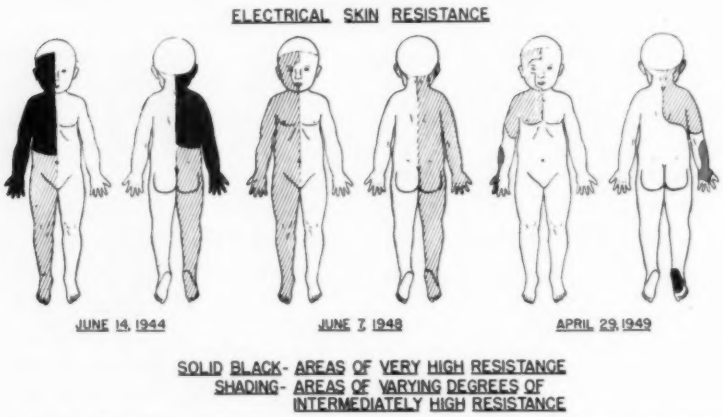
ELECTRICAL SKIN RESISTANCE
JUNE 14, 1944
JUNE 7, 1948
APRIL 29, 1949
SOLID BLACK- AREAS OF VERY HIGH RESISTANCE
SHADING- AREAS OF VARYING DEGREES OF INTERMEDIATELY HIGH RESISTANCE

FIG. 2. Body charts showing the areas of high, intermediately high and normal electrical skin resistance at various stages after the development of the subdural sinus.

April 27, 1949. The examination showed that the area of increased resistance had diminished since the last examination. It included the head (except for facial area), neck, shoulders, part of the arms, and the trunk down to T_5. The increase in resistance was slight but still very definite. To ordinary visual and tactual inspection, however, sweating appeared to be equal on the two sides.

Increased resistance was not found on the trunk and legs, except for an area (solid black) on the plantar surface of the foot. The resistance level of this area was as high as is found after a complete section of a peripheral nerve. In the previous examinations its presence probably was missed.

The electrical skin resistance examinations have shown that the effects produced by the subdural abscess on the sympathetic nervous system may be strictly unilateral. No deviation from normal levels of resistance were observed at any time on the left side of the body, in spite of the presence on that side of definite alteration in sensory and motor functions. The effects produced on the sympathetic nervous system are, in this case, long lasting, being present even after 5 years, however in greatly diminished intensity. They persisted longest in the head and upper thoracic region, the parts of the body farthest removed from the site of the sinus. It is noteworthy that these changes were present in the absence of any abnormalities of the sensory and motor system in this part of the body. The plantar surface of the foot showed an area with an apparently permanent sympathetic denervation.

SUMMARY

This patient was born with an intradural dermal sinus in the lower lumbar and sacral parts of the spinal canal. It drained freely through an opening between the 4th and 5th lumbar vertebrae. At the age of 4 months this draining sinus became infected and at 7 months the excision of the extradural part occluded the sinus and blocked the drainage from the intradural part. The resulting increase of pressure must have first caused the sinus to become very much distended and later may have caused it to rupture, allowing the enclosed pus to spread freely through the subdural space. Pressure from the abscess and/or local inflammatory action on the spinal roots, produced widespread asymmetrical changes in the motor, sensory and autonomical nervous systems. Below T_{11-12} the effects were bilateral, above strictly unilateral.

At the end of the first year drainage of the sinus and treatment with penicillin brought almost immediate relief. The child quickly became able to walk and to carry on many activities. Her bladder control still remained poor. Two years later when all the infection had subsided the intradural part of the sinus was readily removed but some of the sacral roots may have been injured in the process. The child made a rapid recovery. Some sympathetic, motor and sensory changes are however still present but mainly on the right side in this now 5 year old child.

DISCUSSION

An attempt has been made to reconstruct the series of events that led to the changes in the motor, sensory and sympathetic nerves. When the child was first seen the paraplegia and sensory levels (T_4 on right, T_{11} on left) may have been produced by pressure of the distended infected sinus and the subdural abscess on the spinal roots and cauda equina. Some of the damage may also have resulted from direct inflammatory changes in the roots.

The fact that the sensory and sympathetic changes were asymmetrical on the two sides of the body is somewhat disturbing. At one time the loss of sensation extended on the right to T_4; the sympathetic paralysis up to T_1; while similar changes were never higher than T_{11} on the left. It is extremely unlikely that the intradural portion of the dermal sinus extended up the right side of the canal to the upper thoracic region. A subdural abscess however is not restricted in its spread, and could easily have reached that level. It is also not difficult to visualize that it spread higher on one side of the cord than the other. While the infection may have spread that high, the neurological deficits may not have been due to pressure by pus, but may have resulted from an inflammatory reaction. This latter possibility is suggested in view of the slow regression of the sympathetic changes, since alterations in skin resistance were noted in the head and arm long after any pressure from an abscess had been relieved. It might be mentioned that at no time was there evidence for a subarachnoid extension of the infection or for a true myelitis.

Why the sympathetic fibers were so severely injured in the head and arm area, without signs of motor or sensory loss, is not clear. The presence of permanent motor and sympathetic effects in the right foot and saddle region demonstrates that the cauda below L_4 on the right underwent irreversible changes. This may have been due to prolonged pressure from the sinus and abscess, direct infection, or the subsequent arachnoiditis as remarked above. When the intradural portion of the sinus was removed the lumbar and upper sacral roots were not damaged.

Since lesions to nerves at L_3 or below do not produce changes in skin resistance because the sympathetic outflow is complete at L_2, the

changes noted in the right leg must have resulted from injury to the roots at L_1 or L_2. While the roots did not appear abnormal at operation, they could easily have been more or less severely damaged at the time of the acute infection. Here the damage was not so selective, and motor deficits as well as damage to the sympathetic fibers, may have resulted.

As was found in other reported cases, there was remarkable recovery after the infection was brought under control and the sinus removed.

SUMMARY

The history of a patient with congenital intradural dermal sinus is reviewed. During infancy the sinus became infected. Later a partial excision blocked its drainage and led to the formation of a subdural abscess. This was cured by surgical drainage and chemotherapy. At a later date the dermal sinus was completely removed.

Unilateral widespread changes in the sympathetic nervous system were noted during the time of the subdural empyema. These changes were persistant as is evidenced by electrical skin resistance readings taken as long as 4 years after the cure of the abscess.

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BOOK REVIEWS

(These reviews represent the individual opinions of the reviewers and not necessarily those of the members of the Editorial Board of the Bulletin)

Tom Cullen of Baltimore. By JUDITH ROBINSON. 435 pp. $3.50. *Oxford University Press, New York.*

Tom Cullen of Baltimore, Oxford Press, is the biography of the only remaining member of the medical faculty whose professional life span coincides with that of The Johns Hopkins Hospital and Medical School. The eldest son of a Wesleyan minister in the bush country of the newly settled Ontario, Tom Cullen's childhood would seem rugged to the modern child but it was rich in the adventures of boys in a country well suited for the development of self-reliant men. His early education was in the public schools of the smaller communities to which his father was assigned and later in Toronto. Although encouraged at home in his efforts for an education he was forced to support himself from an early age. Even while attending medical school in Toronto his earnings from his paper route and other tasks paid his tuition and other expenses. In reading of his early life it is apparent that the tremendous drive and capacity for work which characterized his later years began at a very early age. His habit of early rising to work before breakfast, although modified gradually with passing years, remained with him throughout life.

The dynamic push which was one of Dr. Cullen's most characteristic qualities did not exclude play. He received a tremendous amount of pleasure from his work and enjoyed a little horseplay at the operating table as much as his younger assistants. In addition he was an ardent advocate of prolonged summer vacations and one of his commonest admonitions to young men was, "Remember you can do more work in ten months than in twelve". As soon as his financial position made it possible he spent two full months at his camp on Lake Ahmic in the Magnetawan country of Ontario. But on returning in September his drive for work was unremitting until the following July.

In 1891 young Tom Cullen came to Baltimore as an interne under Dr. Kelly. From that moment on, his "chief" became his hero and remained so until Kelly's death. With almost dog-like faithfulness he carried out the "chief's" wishes even when he had to swallow hard to accept some of Kelly's views. After completing his training as a gynecologist Cullen's professional life was spent in Baltimore and eventually he succeeded his master as Chief Gynecologist of The Johns Hopkins Hospital and as Professor of Gynecology of The University. He served in this dual capacity until he reached the age of retirement in 1939. In the two decades during which Cullen occupied the Chair of Gynecology, Hopkins was torn with family feuds in which Cullen was embroiled. The biographer tells the story of the fight on full time professorships which divided the faculty sharply into two camps.

She also relates the gynecological-obstetrical feud in which Cullen and Williams played leading roles. After the passage of many years these stories are told without rancor but let the reader not be misled into believing that it did not exist at the time.

Cullen's greatest contribution to gynecology was his development of the gynecological pathology laboratory. The interest which he inspired in this phase of gynecology has had a more profound and important influence on his specialty than any of his other accomplishments. Another accomplishment of almost equal importance to medicine was the work he did single-handedly in establishing a Chair of Medical Art at the Hopkins. This chair was occupied with distinction for many years by his devoted friend, Max Brödel, whose work established art as applied to medicine in this country.

It is regrettable that the biography, which in a sense is a history of the Hopkins gynecological department does not tell more of the accomplishments of Cullen's co-workers in the development of this department.

On the occasion of his seventieth birthday Tom Cullen's friends gave a testimonial dinner to him which was attended by a host of friends and admirers. This was the end of his University life but not of his career. He continued actively in practice and made his greatest contribution to the City of Baltimore as President of the Board of the Enoch Pratt library. He was elected to this post in 1938 and his faithful performance of his duties and great enthusiasm for the cause have resulted in his re-election each year since.

The book is written in a readable style by Judith Robinson. Her style is light enough to be entertaining and factual enough to be of value as an historical document covering an important and long era in The Johns Hopkins Medical Institutions. Much of it is in direct quotation by Tom Cullen in his inimitable style. His personality almost steps out of the pages. To all Hopkins alumni, to Baltimore citizens and to Tom Cullen's many friends throughout the country the volume will prove to be highly pleasing reading.

R. W. Te Linde

The Diagnosis of Pancreatic Disease. By Louis Bauman. 74 pp. $5.00. *J. B. Lippincott Co. Philadelphia.*

The diagnosis of disease of the pancreas is always difficult. Within the last few years a number of studies have appeared in which the enzymatic properties of pancreatic juice have been analyzed as a diagnostic aid. Dr. Bauman, in this monograph, summarizes his experience in the laboratory diagnosis of pancreatic disease. Briefly, Bauman's technique consisted of passing a double-barrelled tube into the duodenum. Through one half of the tube, the pancreatic juice was aspirated. Through the other half, the gastric juice was neutralized by calcium carbonate. The duodenal juice was collected in 10 minute fractions into iced receiving tubes, and analyzed for its content of amylase, protease, and lipase. Mecholyl was used as a stimulant of pancreatic secretion because secretin was expensive, and tended to be toxic.

Dr. Bauman does not believe that one should aspirate the pancreatic juice to assist in the diagnosis of acute pancreatitis, although others have reported a deficiency in amylase and protease in this disease. In chronic pancreatitis and carcinoma of the head of the pancreas, Bauman observed that the concentration of pancreatic enzymes was decreased. However, in cancer of the body of the pancreas, he found that the pancreatic enzymes were usually normal.

In interpreting Dr. Bauman's data, one must bear in mind that the great variations in enzymatic activity are observed in patients who apparently do not have pancreatic disease. Moreover, the data presented indicate that mecholyl is a poor stimulant of the flow of lipase in most patients. In his discussion of sprue, Dr. Bauman confirms the fact that the pancreatic secretions in this disease are usually normal. He does not remark that half of his patients had a fasting level of lipase which was less than the minimum normal value. The significance of this observation is not clear.

This small volume is well-written and is published in the most attractive way. However, it seems unnecessary to charge $5.00 for a book which is 74 pages in length. Undoubtedly the large amount of tabular material which is presented is difficult to set. However, a less expensive format and binding, might have permitted making this valuable little book more attractively priced and therefore more accessible to the average medical reader.

OSCAR D. RATNOFF, M.D.

Physiology in Diseases of the Heart and Lungs. M. D. ALTSCHULE. 368 + XV pp. $5.00 *Cambridge, Harvard University Press*, 1949.

The author, who has contributed many precise measurements, analyses and speculations to the field embraced by his book, has now written a monograph which is difficult to classify. In the preface there is outlined the goal of providing the student (pre- or postdoctoral) with source material derived from laboratory and clinical research so that, "The student may be stimulated to look into this book for the explanation of an unusual or, to him, unexpected clinical phenomenon, or he may merely browse through it when he feels no urge to do anything else." There can be no cavil at this aim which responds to an urgent need.

In order to provide this material the author has written a series of brief essays within the framework of more inclusive disease patterns. For example, the first section on *chronic cardiac decompensation* occupies 217 pages consisting of 37 essays on such topics as cardiac output, venous pressures, respiratory dynamics, extracellular fluid volume, renal function, skeletal muscle function, cyanosis, etc. The following 85 pages are devoted to other patterns of cardiac disease. The last 52 pages are devoted to several representative diseases of the respiratory apparatus.

The style of these brief essays is determined by the author's decision to provide almost encyclopedic references to the vast body of observations recorded, for the most part, in the past 40 years. Thus, an average page is peppered with 20 or more references. This does not make easy reading. Each brief section is followed by a bibliography often occupying four to five pages.

The enormous value of this careful work is the provision of what is virtually an annotated bibliography with sensible, critical evaluation. For the thoughtful student, many bare statements may be too elliptical to be satisfying. Perhaps this will stimulate reference to the original reports which are listed in such generous profusion. If this be the case, one goal will have been reached.

It is probably a reflection of the fluidity of the subject that appears in these essays as an unwelcome similarity to some of the synoptic reviews of recent years. Despite these lesser shortcomings, this book is recommended without reservation to all physicians and biologists concerned in any fashion with problems of circulation and respiration.

J. L. L., Jr.

Medical Clinics on Bone Diseases, 2nd edition. By I. Snapper. 292 pp. $20.00. *Interscience Publishers, Inc. New York 3, N. Y.*

This profusely illustrated and documented atlas and text emphasizes the metabolic aspects of the etiology of bone diseases. It follows that knowledge concerning the changes brought about by hyperparathyroid disease and by hyperplasia of the parathyroids secondary to kidney disease are given great prominence. Bony changes secondary to multiple myeloma, to various anemias, Gaucher's disease are considered in detail. Illustrations of osteosclerotic and osteoclastic responses in Hodgkin's are striking. A valuable feature is the case reports, some from the literature, many from the author's own experience. A good book such as this might be even more valuable had it included some reference to tumors of the bone, osteomyelitis and syphilis. However, the author does not pretend to complete coverage.

Taxonomists of insects are frequently listed as "splitters" or "lumpers" in their consideration of the specific and generic relations of the various species. Dr. Snapper is apparently a "lumper" when it comes to the varieties of lesions described in bone diseases. This, no doubt, is good when dealing with a poorly understood group. One wishes, however, that eponyms had been used at an absolute minimum. Actually we frequently find some worthy investigator's name attached to the cells, the symptoms or signs and the disease complex.

This is, however, a good and worthwhile book, which will serve as a frequent reference in any large medical clinic.

F. B. B.

A Textbook of Neuropathology. By Ben W. Lichtenstein, B.S., M.S., M.D. *Published by W. B. Saunders Company, Philadelphia and London,* 1949. pp. 474. $9.50.

As the author mentions in his preface, this new book has been prepared primarily for the medical student. He introduces the reader to alterations in structure of the nervous system in a satisfactory general fashion. Tissue changes are discussed primarily in terms of possible causative factors rather than as discrete disease entities. Of necessity, this form of presentation leads to rather artificial

grouping in some instances. Controversial subjects are minimized. The author is found adding many short inadequate descriptions of far too many rare, or not so rare, entities which don't quite fit in. Thumbnail sketches of clinical topics keep appearing in a fashion which might lead to confusion. These adornments, like the brief chapter on neuroanatomy seem far too inadequate and might well have been omitted.

It is unfortunate that these features tend to detract from the fundamental value of this book. The general plan and treatment is good, and much needed. The writing is clear and interesting. The illustrations are, in most cases, excellent.

J. W. M.

The Practice of Refraction. By SIR STEWART DUKE-ELDER. 5th Edition. Illus. 290 pp. $6.25. *The C. V. Mosby Company, St. Louis, Missouri,* 1949.

This new edition has been thoroughly revised and brought up to date while preserving the size of the previous editions. The original lucid style used in describing the principles of refraction has been maintained.

Data on the variability of the axial length of the eyeball, as determined roentgenologically, has been added. The section on anomalies of refraction has been expanded to include a more thorough description of aniseikonia and of transient changes in refraction. New material also has been added to the sections dealing with the accommodation-convergence mechanism, with heterophoria and with contact lenses.

Sir Stewart Duke-Elder's book well deserves its popularity and certainly will maintain its position as one of the foremost textbooks on refraction.

W. G. M.

Care of the Surgical Patient. By JACOB FINE. *W. B. Saunders Co., Philadelphia,* 1949. 544 pages. $8.00.

There is a great deal of wisdom and much sound advice in this lucid and comprehensive book. The style and the treatment are rapid and conversational. An astonishing amount of ground is covered. There are good sections on fluid balance and nutrition; sections covering a great diversity of conditions in all the special fields and types of surgery; sections on laboratory methods and special sections on the general aspects of preoperative and postoperative care. The treatment of most sections is of necessity didactic and brief; references are few and no bibliography is given. The book will be most useful to the student or practitioner interested in a rapid review such as might be given in a lecture series.

M. M. R.

Male and Female. By MARGARET MEAD. 477 pp. $5.00. *William Morrow & Co. New York 16.*

Margaret Mead believes that the quality of our civilization is threatened, because we falsely delimit maleness and femaleness, and that human culture will

progress or decay only so far as we use the gifts and respect the inherent differences peculiar to each sex.

One threat to our full cultural growth is the tendency to limit certain professional, intellectual and familial practices to one sex and as a corollary to impose a social penalty on the other sex for participation in that practice. Dr. Mead examines fully, and fairly, the physical and the learned differences between male and female and pleads for careful judgment in whatever changes we make in recreating the tasks of both as we build for the future. The American marriage ideal is almost impossibly difficult to maintain, based as it is on romantic love, financial security and spiritual fidelity, and it can achieve stability only by complete mutual respect for the mind, body, and ideals of the co-partner.

Anthropology is the logical discipline from whence a warning to pause and take stock of our social development should come. Dr. Mead analyzes the swift changes in our culture against a background of seven South Sea cultures whose biological equipment and basic heritage are the same as ours. Sexual intercourse is immensely enjoyed by the Samoans, detested by the cannibal Mundugumor of New Guinea, tolerated as an economic necessity by other peoples, and set in a graceful ritual by the Balinese. And, just as the sex act itself is affected by customs locally imposed, so is the way of life of the people a reflection of their attitude toward the role of male and female.

In our country the pattern of contemporary living is affecting the basic biological cycle. Wars have left a surplus of women, the rearing of children and the life of the family has become a matter of keeping up with the Joneses in double harness, while observing obscurely defined taboos in business and in intellectual pursuits.

One world, unified by technology, and in a gradually levelling intellectual environment, is on the horizon. Dr. Mead would have us stop, while we can still alter the blueprints, and think on these things.

B. G. B.

Medical Etymology. By O. H. PERRY PEPPER. 263 pp. $5.00. *W. B. Saunders Co., Phila., Pa.*

This interesting attempt at furthering one phase of medical education and easing the burden of the medical student will meet a varied reception. It is a welcome guide to the meaning—from the etymological point of view—of medical words. Despite the necessary interest in eponyms, one welcomes the author's statements that "eponymic titles are given to diseases only for lack of something better . . . eponyms persist and defy the advance of knowledge, but must always lose out in the end, when science learns enough to justify the coining of some appropriate term. Often an eponym is a clear indication of our ignorance and constitutes a challenge to the investigator to rid our terminology of one more eponym".

The book is in no sense a dictionary. No attempt is made even to tell you that Aedes and Anopheles are mosquitoes—only that Aedes means unpleasant and

Anopheles harmful, and furthermore to discover this, the reader must know that he should look under the parasitology section.

There are errors and inadequacies. For instance, the statement "*variolation*, meaning to vaccinate with cowpox virus" and under *Giardia* the inference that this is a worm. The entire definition of trophozooite as "a stage of the malarial parasite" would be misleading to the student, who was at the time reading about amoebiasis.

Despite such scattered inconsistencies, this is a good book and a worthwhile attempt.

F. B. B.

BOOKS RECEIVED FOR REVIEW

A Year with Osler. By JOSEPH H. PRATT. 209 pp. $4.00. *The Johns Hopkins Press, Baltimore, Md.*

Atlas of Obstetric Technic, 2nd edition. By PAUL TITUS. 197 pp. $7.50. *The C. V. Mosby Co., St. Louis, Missouri.*

Tom Cullen of Baltimore. By JUDITH ROBINSON. 435 pp. $3.50. *Oxford University Press, N. Y.*

Fundamentals of Otolaryngology. By LAWRENCE R. BOIES. 443 pp. $6.50. *W. B. Saunders Co., Philadelphia, Pa.*

Haemoglobin. By F. J. W. ROUGHTON AND J. C. KENDREW. 317 pp. $8.50. *Interscience Publishers, N. Y. 3*

Histopathology of the Skin. By WALTER F. LEVER. 449 pp. $10.00. *J. B. Lippincott Co., Philadelphia, Pa.*

Industrial Hygiene and Toxicology, vol. 2. By FRANK A. PATTY. 1138 pp. $15.00. *Interscience Publishers, N. Y. 3*

Life Among the Doctors. By PAUL DE KRUIF. 470 pp. $4.75. *Harcourt, Brace & Co., N. Y. 17.*

Male and Female. By MARGARET MEAD. 477 pp. $5.00. *William Morrow & Co., N. Y. 16,*

Marihuana in Latin America. The Threat it Constitutes. By PABLO OSVALDO WOLFF. 56 pp. $1.50. *Washington Institute of Medicine (sponsors) Linacre Press, Inc., Washington 6, D. C.*

Medical Clinics on Bone Diseases, 2nd edition. By I. SNAPPER. 292 pp. $20.00. *Interscience Publishers, Inc., N. Y. 3*

Nervous and Neurohumoral Regulation of Intestinal Motility. By W. B. YOUMANS. 129 pp. $4.75. *Interscience Publishers, Inc., N. Y. 3*

Operations of General Surgery, 2nd edition. By THOMAS G. ORR. 890 pp. $13.50. *W. B. Saunders Co., Philadelphia, Pa.*

Physiology in Diseases of the Heart and Lungs. By MARK D. ALTSCHULE. 368 pp. $5.00. *Harvard University Press, Cambridge, Mass.*

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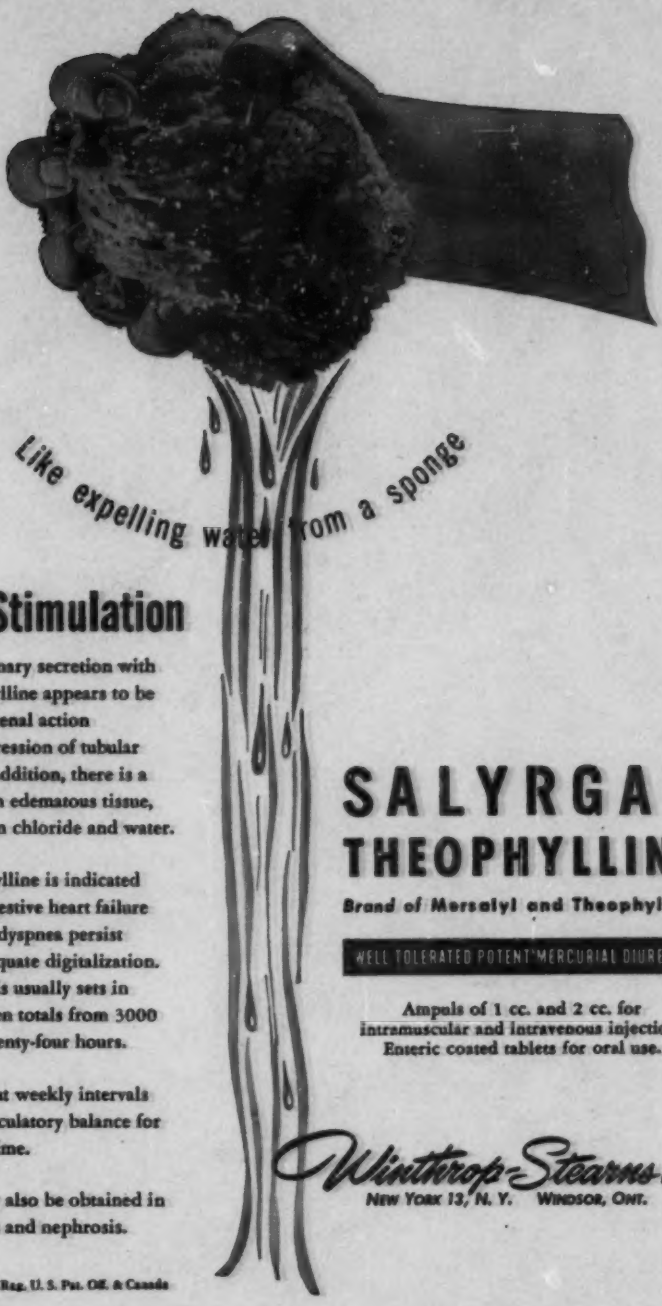

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Stimulation of urinary secretion with Salyrgan-Theophylline appears to be due chiefly to its renal action consisting of depression of tubular reabsorption. In addition, there is a direct influence on edematous tissue, mobilizing sodium chloride and water.

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